biomedical diagnostics

Premarket Notification 510(k) Summary

Assigned 510(k) Number: K070458

DEC 2 1 2007

1) Submitted by :

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2) Device Name

Trade/Proprietary Name :	**FIDIS™ VASCULITIS Assay kit**
Common/Usual Name :	**MX007 - FIDIS™ VASCULITIS**: Detection test for autoantibodies directed against Myeloperoxidase (MPO), Serine Proteinase 3 (PR3) and Glomerular Basement Membrane (GBM) in human serum
Classification Names:	Test system, Antineutrophil Cytoplasmic Antibodies (ANCA) Devices, Measure, Antibodies to Glomerular Basement Membrane (GBM)
Trade/Proprietary Name :	**FIDIS™ Analyzer**
Classification Name:	Instrumentation for Chemical Multiplex Systems
Trade/Proprietary Name :	**CARIS™ System**
Classification Name:	Device, Microtiter diluting/Dispensing

3) Intended use

The **FIDIS™ VASCULITIS*** kit is a semi-quantitative homogeneous fluorescent-based microparticle immunoassay using flow cytometry. The test system is used to simultaneously detect the presence of anti-neutrophil cytoplasmic antibodies (ANCA) directed against Myeloperoxidase (*MPO*), Serine Proteinase 3 (*PR3*) and antibodies directed against glomerular basement membrane (GBM) in human serum samples.

The results of the **FIDIS™ VASCULITIS*** test are to be used in conjunction with the clinical findings and the other laboratory tests to aid in the diagnosis of various primary systemic small blood vessel vasculitides and glomerular basement membrane disease.

Clinical utility:

The detection of ANCA is associated with primary systemic small blood vessel vasculitides: Wegener's granulomatosis, Churg Strauss syndromes, microscopic periarteritis and idiopathic crescentic glomerulonephritis; and the detection of anti-GBM antibodies is associated with Goodpasture's syndrome.

FIDIS™ VASCULITIS* kit uses serum only, and is to be run on the FIDIS™ Instrument and MLX-BOOSTER Software.

FIDIS™ VASCULITIS* kit may be used with the **CARIS™ system** (diluting and dispensing device).

This test is for *In vitro* diagnostic use.

* Detection of the serologic markers for primary systemic small blood vessel vasculitides (ANCA) and for Goodpasture syndrome (GBM).

4) Materials supplied

1 x 96 wells microplate including a filtering membrane and a lid.	1 plate
1 vial **(A)** of 3 sets of color-coded microsphere beads coupled with MPO, PR3 and GBM*, plus 1 set of internal standard beads. Ready to use	1 x 6mL
1 vial **(B)** of sample dilution buffer (PBS-Tween) (white vial) Ready to use	2 x 115mL
1 vial of calibrator** titered for the specificities to be measured. Ready to use ***Each titer is printed on the vial label***	1 x 1,5mL

1 vial of positive control** concentrate. This control has a standard reactivity that provides evidence of the proper functioning of reagents and correct assay performance. To be diluted ***Expected values are printed on the vial label.***	1 x 250 µL
1 vial of negative control** concentrate. To be diluted	1 x 250µL
1 vial of anti-human IgG coupled to phycoerythrin Ready to use	1 x 12mL
1 vial (C) of washing buffer (PBS-Tween) (black vial) Ready to use	1 x 100mL
Package Insert	1
Microplate Assay Configuration Worksheet	1
Microplate sealing films	6

* GBM antigen purified from type IV collagen.
** Calibrator and control titers are expressed in arbitrary units per mL (AU/mL).

5) Predicate Device

510K Number	Device Classification Name	Manufacturer Name
K053012	**FIDIS™ VASCULITIS**	Biomedical Diagnostics S.A.(bmd)

6) Comparison with the predicate

		Predicate Device FIDIS™ VASCULITIS K053012	Modified Device FIDIS™ VASCULITIS
Intended use		Individual determination in human serum, of IgG antibodies against: MPO, PR3 and GBM	Same
Antigen		- MPO: purified antigen - PR3: purified antigen - GBM: purified antigen	Same
CUT-OFF	**Negative**	<20 AU/mL for the 3 specificities	Same
	Equivocal	20-25 AU/mL for the 3 specificities	Same
	Positive	>25 AU/mL for the 3 specificities	Same
Material supplied		Microplate with caps	Microplate with sealing films (no change in function and provides flexible use)
Sample dilution		PBS-Tween concentrated	Sample dilution buffer – same ingredients but ready to use
Wash buffer		PBS-Tween concentrated	Washing buffer – same ingredients but ready to use

	Predicate Device FIDIS™ VASCULITIS K053012	Modified Device FIDIS™ VASCULITIS
Internal standard beads	No	Yes
Assay configuration	1 "reagent-blank" well 1 "calibrator" well 1 "negative control" well 1 "positive control" well	1 "reagent-blank" well 1 "negative control" well 1 "positive control" well 2 "calibrator" wells
	Diluted sample wells	Same
	A second calibrator well every 32 well series	No
Incubation time	2 x 30mn RT	Same
Assay protocol	Optional final wash step	Final wash step (not optional)
Software	MLX-Booster Version 1.35	MLX-Booster Version 2.2
Assay technology	Flow cytometric	Flow cytometric
Sample delivery	Manual pipetting	Same
Automated sample delivery (option)	CARIS™ (pipettor)	Same

7) Performance Characteristics

1. Analytical performance

a. Precision

Precision of the assay was assessed in **16 samples** for antibodies to each of the three analytes (MPO, PR3, GBM) and **3 negative samples**. Precision was determined by calculating the within-run (intra-assay) and the between run (inter-assay).

- For within-run: 10 tests in a same run.
- For between-run: 5 runs, 3 tests per run.

Table 1: Summary of FIDIS™ Vasculitis precision results

Sample range	Acceptance criteria for within-run and between-run	MPO, PR3 and GBM parameters			
		Within-run		Between-run	
		Minimal %CV	Maximal %CV	Minimal %CV	Maximal %CV
Less than 10 AU/mL	**Not calulated**	Not calculated	Not calculated	Not calculated	Not calculated
10 to 19 AU/mL	**%CV≤20%**	5.3%	11.3%	11.2%	19.6%
20 to 400 AU/mL	**%CV≤15%**	2.3%	12.4%	5.4%	14.2%

b. Linearity/ assay reportable range

FIDIS™ VASCULITIS assay has been optimized to express the average binding capacity at the current dilution (1:200) by a flow cytometric reading determined as the median fluorescence value obtained from 200 microspheres per parameter.

Further dilution potentially gives rise to inaccurate results because the reaction conditions and the equilibrium of the immunological reaction may be modified.

c. Interfering Substances

The study was conducted by testing 27 MPO, PR3, GBM negative samples characterized as positive for various potential interferences obtained from a routine laboratory.

Table 2: Summary of Interfering Substance results

	Number of positive samples		
	MPO	PR3	GBM
Cryoglobulinemia N=2	0	0	0
Complement N=8	0	0	0
IgG monoclonal immunoglobulins N=2	0	0	0
IgM monoclonal immunoglobulins N=3	0	0	0
Rheumatoid factor N=7	0	1	0
Citrated plasma N=3	0	0	0
Hemolyzed sera N=2	0	0	0

N: number of samples tested

d. Threshold values

Threshold values were estimated from the 2 selected populations:

- 37 samples from blood donors
- 28 samples selected for their potential biological interferences

The negative thresholds (20AU/mL) correspond to the 100% of negative MPO/GBM samples and 98.5% of negative PR3 samples for the populations studied.

e. Stability of the assay results after final wash step

This assay included 3 test series for **6 samples** per analyte (MPO, PR3, GBM). Each series of tests was washed and read after different times:

- T= 0 hour: the first series of tests was read immediately after the final wash step.
- T= 4 hours: the second series of test was read after 4 hours of storage at room temperature away from direct sunlight.

- T=18 hours: the last series was read after 18 hours of storage at room temperature away from direct sunlight.

Table 3: Summary of Stability of the assay results after final wash step

%CV acceptance criteria	Parameter	Sample	Mean (AU/mL)	%CV
CV%<15%	MPO	Sample 1	19	14%
		Sample 2	32	6%
		Sample 3	45	4%
		Sample 4	92	4%
		Sample 5	156	12%
		Sample 6	260	8%
	PR3	Sample 7	23	11%
		Sample 8	29	3%
		Sample 9	50	3%
		Sample 10	106	10%
		Sample 11	231	8%
		Sample 12	834	6%
	GBM	Sample 13	78	5%
		Sample 14	79	5%
		Sample 15	108	6%
		Sample 16	129	5%
		Sample 17	150	7%
		Sample 18	213	5%

- Based on the common laboratories practices, the time range recommended is "one hour for a plate when stored at room temperature away from direct sunlight".

2. Comparison study with predicate

bmd has compared the results obtained with **modified FIDIS™ VASCULITIS** versus the results obtained with **predicate FIDIS™ VASCULITIS K053012.**

The study was performed on 219 samples characterized with the predicate test and the result repartition is described below:

- **135 samples were positive** for one or more parameters ANCA and/or GBM.
- **84 negative samples** including some samples **evaluated for their potential biological interferences.**

All equivocal samples with predicate and **FIDIS™ VASCULITIS tests** are considered negative for the comparison and the evaluation studies.

⇨ **Table 4: MPO performances**

MPO		PREDICATE FIDIS™ VASCULITIS K053012		
		Positive	Negative	Total
MODIFIED FIDIS™ VASCULITIS	Positive	69	0	69
	Negative	2	148	150
	Total	71	148	219

There were 7 equivocal results with the assay. For purposes of calculation, these results were considered as negative.

- **Positive percent agreement: 97.18% (69/71)**
- **Negative percent agreement: 100% (148/148)**
- **Overall agreement: 99.09% (217/219)**

⇨ **Table 5: PR3 performances**

PR3		PREDICATE FIDIS™ VASCULITIS K053012		
		Positive	Negative	Total
MODIFIED FIDIS™ VASCULITIS	Positive	47	1	48
	Negative	2	169	171
	Total	49	170	219

There were 11 equivocal results with the assay. For purposes of calculation, these results were considered as negative.

- **Positive percent agreement: 95.92% (47/49)**
- **Negative percent agreement: 99.41% (169/170)**
- **Overall agreement: 98.63% (216/219)**

⇨ **Table 6: GBM performances**

GBM		PREDICATE FIDIS™ VASCULITIS K053012		
		Positive	Negative	Total
MODIFIED FIDIS™ VASCULITIS	Positive	25	0	25
	Negative	0	194	194
	Total	25	194	219

There were 3 equivocal results with the assay. For purposes of calculation, these results were considered as negative.

- **Positive percent agreement: 100% (25/25)**
- **Negative percent agreement: 100% (194/194)**
- **Overall agreement: 100% (219/219)**

Table 7: Summary of performance agreement results

Antigenic Specificity	Sample number	Positive percent agreement	Negative percent agreement	Overall agreement
		proportion	proportion	proportion
MPO	**219**	97.18%	100%	99.09%
PR3	**219**	95.92%	99.41%	98.63%
GBM	**219**	100%	100%	100%

In addition to the analysis above, the 95% one-sided lower confidence limit in percent of proportion agreement (95% LCL (%) was calculated using the Exact Binomial Test for proportions to determine how low this proportion could be with a 95% confidence.

Table 7a: Summary of performance agreements results - 95% LCL (%)

Antigenic Specificity	N	Positive Agreement				Negative Agreement				Overall Agreement			
		N_1	R_1	P_1 (%)	95% LCL (%)	N_2	R_2	P_2 (%)	95% LCL (%)	N	R	P (%)	95% LCL (%)
MPO	219	71	69	97.18	91.40	148	148	100.00	98.00	219	217	99.09	97.15
PR3	219	49	47	95.92	87.70	170	169	99.41	97.24	219	216	98.63	96.50
GBM	219	25	25	100.00	88.71	194	194	100.00	98.47	219	219	100.00	98.64

N_1 = No. of positives; R_1 = No. of positive agreements; $P_1 = R_1/N_1$
N_2 = No. of negatives; R_2 = No. of negative agreements; $P_2 = R_2/N_2$
$N = N_1 + N_2$; $R = R_1 + R_2$; $P = R/N$

All of results show that **FIDIS™ VASCULITIS system** can be considered substantially equivalent to the predicate **K053012 FIDIS™ VASCULITIS system.**

3. Performance data for modified FIDIS™ VASCULITIS with CARIS™ (diluting/ dispensing Device)

a. Precision

Internal study was conducted to evaluate the reproducibility of the use of **CARIS™ with modified FIDIS™ VASCULITIS.**

Precision of the assay was assessed in **16 samples** for antibodies to each of the three parameters (MPO, PR3, GBM) and **3 negative samples**. Precision was determined by calculating the within-run (intra-assay) and the between-run (inter-assay).

Precision was determined by calculating the within-run (intra-assay) and the between-run (inter-assay).

- For within-run: 10 times in a same run.
- For between-run: 5 runs, 3 times per run.

Table 8: Summary of CARIS™ precision results

Sample range	Acceptance criteria for within-run and between-run	Within-run minimal CV% for MPO, PR3 and GBM parameters	Within-run maximal CV% for MPO, PR3 and GBM parameters	Between-run minimal CV% for MPO, PR3 and GBM parameters	Between-run maximal CV% for MPO, PR3 and GBM parameters
Less than10 AU/mL	Not calculated	Not calculated	Not calculated	Not calculated	Not calculated
10 to 19 AU/mL	CV=20%	4.9%	6.9%	6.9%	13.6%
20 to 400 AU/mL	CV=15%	2.6%	10.8%	5.9%	11.7%

b. Comparison studies (manual versus automated assay preparation steps)

bmd has compared the results obtained with **modified FIDIS™ VASCULITIS** for **manual or automated (with CARIS™).**assay preparation steps.

The study was performed on 117 samples characterized with the **modified FIDIS™ VASCULITIS** with **manual** assay preparation step.
The result repartition is described below:

- 75 **positive samples** for one or more parameters ANCA and/or GBM.
- 42 **negative samples** including some samples **evaluated for their potential biological interferences**.

All equivocal samples are considered negative for the comparison and the evaluation studies.

⇨ **Table 9: MPO performances**

MPO		MODIFIED FIDIS™ VASCULITIS Manual		
		Positive	Negative	Total
MODIFIED FIDIS™ VASCULITIS With CARIS	Positive	34	2	36
	Negative	0	81	81
	Total	34	83	117

There were 5 equivocal results with the assay. For purposes of calculation, these results were considered as negative.

- **Positive percent agreement: 100% (34/34)**
- **Negative percent agreement: 97.59% (81/83)**
- **Overall agreement: 98.29% (115/117)**

⇨ **Table 10: PR3 performances**

PR3		MODIFIED FIDIS™ VASCULITIS Manual		
		Positive	Negative	Total
MODIFIED FIDIS™ VASCULITIS With CARIS	Positive	25	2	27
	Negative	0	90	90
	Total	25	92	117

There were 6 equivocal results with the assay. For purposes of calculation, these results were considered as negative.

- **Positive percent agreement: 100% (25/25)**
- **Negative percent agreement: 97.83% (90/92)**
- **Overall agreement: 98.29% (115/117)**

⇨ **Table 11: GBM performances**

GBM		MODIFIED FIDIS™ VASCULITIS Manual		
		Positive	Negative	Total
MODIFIED FIDIS™ VASCULITIS With CARIS	Positive	23	0	23
	Negative	0	94	94
	Total	23	94	117

There were 3 equivocal results with the assay. For purposes of calculation, these results were considered as negative.

- **Positive percent agreement: 100% (23/23)**
- **Negative percent agreement: 100% (94/94)**
- **Overall agreement: 100% (117/117)**

Table 12: Summary of performance agreements results obtained with CARIS™ versus manual

Antigenic Specificity	Sample number	Positive percent agreement	Negative percent agreement	Overall agreement
		proportion	proportion	proportion
MPO	117	100%	97.59%	98.29%
PR3	117	100%	97.83%	98.29%
GBM	117	100%	100%	100%

In addition to the analysis above, the 95% one-sided lower confidence limit in percent of proportion agreement (95% LCL (%) was calculated using the Exact Binomial Test for proportions to determine how low this proportion could be with a 95% confidence.

Table 12a: Summary of performance agreements results obtained with CARIS™ versus manual - 95% LCL (%)

Antigenic Specificity	N	Positive Agreement				Negative Agreement				Overall Agreement			
		N_1	R_1	P_1 (%)	95% LCL (%)	N_2	R_2	P_2 (%)	95% LCL (%)	N	R	P (%)	95% LCL (%)
MPO	117	34	34	100.00	91.57	83	81	97.59	92.61	117	115	98.29	94.72
PR3	117	25	25	100.00	88.71	92	90	97.83	93.31	117	115	98.29	94.72
GBM	117	23	23	100.00	87.79	94	94	100.00	96.86	117	117	100.00	97.47

N_1 = No. of positives; R_1 = No. of positive agreements; $P_1 = R_1/N_1$
N_2 = No. of negatives; R_2 = No. of negative agreements; $P_2 = R_2/N_2$
$N = N_1 + N_2$; $R = R_1 + R_2$; $P = R/N$

All of previous evaluation results indicate that manual and automated **(with CARIS™)** assay preparation steps are substantially equivalent.

8) Conclusions

In conclusion, all supporting data demonstrate that the **FIDIS™ VASCULITIS system** can be considered substantially equivalent to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 2 1 2007

Biomedical Diagnostics S.A. (BMD)
c/o Ms. Christelle Courivaud
Regulatory Affairs Manager
Actipole 25,
4-6 Bld de Beaubourg
77435 Marne La Vallée cedex 2
France

Re: k070458
Trade/Device Name: FIDIS™ VASCULITIS* Assay
Regulation Number: 21 CFR 866.5660
Regulation Name: Multiple autoantibodies immunological test system
Regulatory Class: Class II
Product Code: MOB, MVJ
Dated: November 27, 2007
Received: November 30, 2007

Dear Ms. Courivaud:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to

begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Robert L. Becker, Jr., M.D., Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K070458

Device Name: **FIDIS™ VASCULITIS***

Indication For Use:

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FIDIS™ VASCULITIS* kit uses serum only, and is to be run on the FIDIS™ Instrument and MLX-BOOSTER Software.

FIDIS™ VASCULITIS* kit may be used with the **CARIS™ system** (diluting and dispensing device).

This test is for *In vitro* Diagnostic Use.

* Detection of the serologic markers for primary systemic small blood vessel vasculitides (ANCA) and for Goodpasture syndrome (GBM).

Prescription Use ___X___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Maria M Chan

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety
510(k) 070458